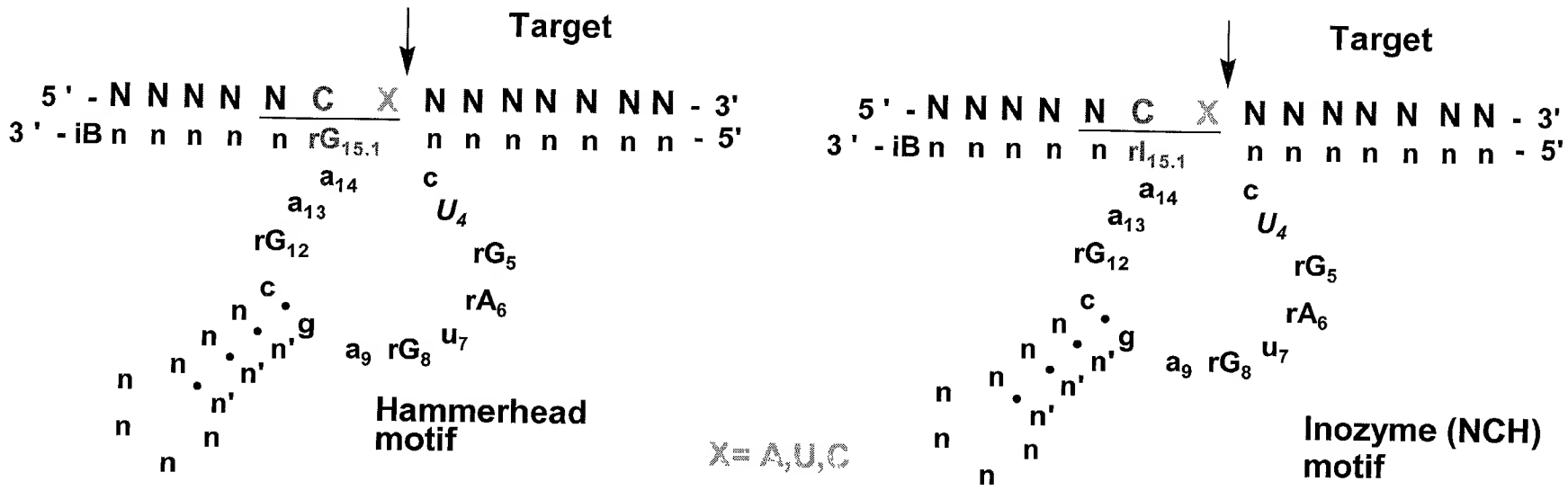
Figure 1: Examples of Chemically Stabilized Enzymatic Nucleic Acid motifs



Lower case = 2'-*O*-Me

rN = ribonucleotide

U_4 = 2'-*C*-Allyl

rI = ribo Inosine modification

iB = inverted deoxy abasic

Figure 2: G-cleaver Motif

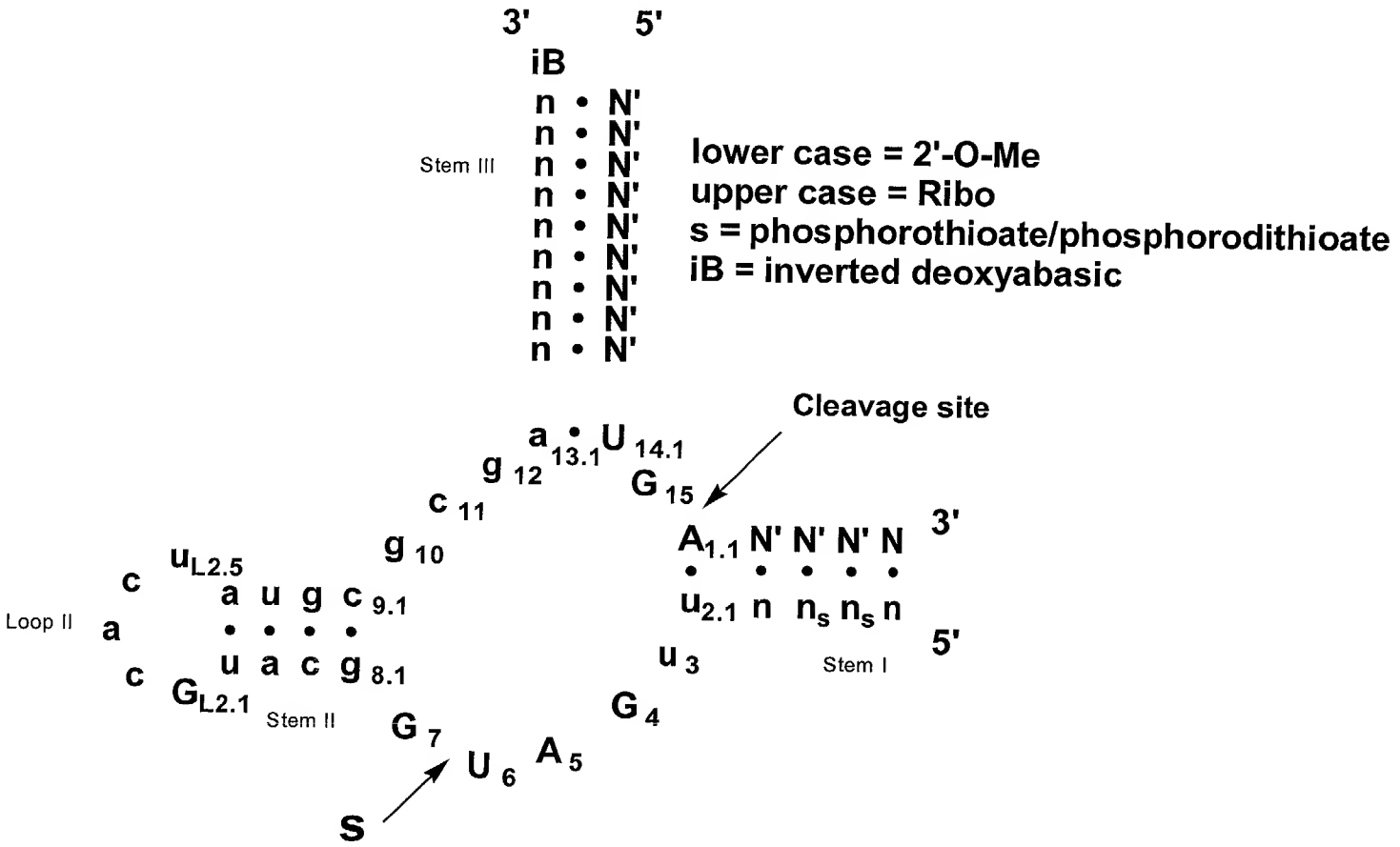
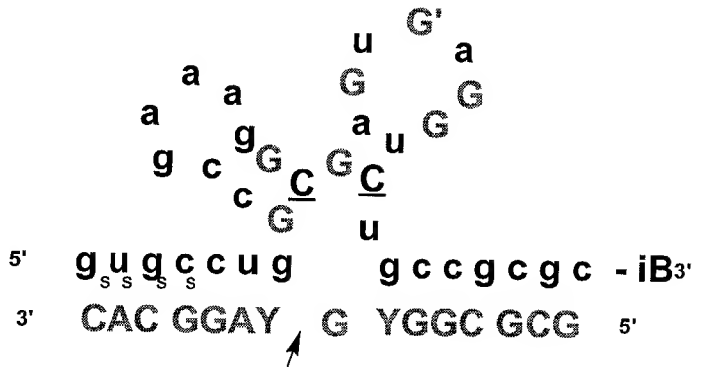


Figure 3: Chemically Stabilized Zinzyme Motif



Legend

Uppercase indicates natural ribo residues

C indicates 2'-deoxy-2'-amino cytidine

Lowercase: 2'-*O*- Me

Subscript $_S$ indicates phosphothioate linkage

iB: 3'-3' abasic moiety

Y = U or C

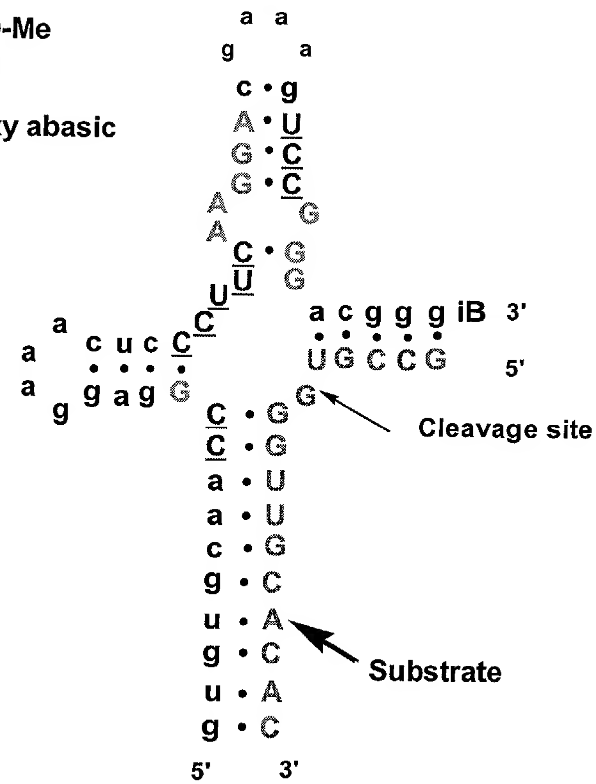
G' can be G, ca, or caa

The gaaa tetraloop can be replaced by 18 atom polyethylene glycol (Spacer) or equivalent

All ribo G's in the Zinzyme can be replaced with 2'-*O-methyl* G, or combinations thereof

Figure 4. Chemically Stabilized Amberzyme Motif

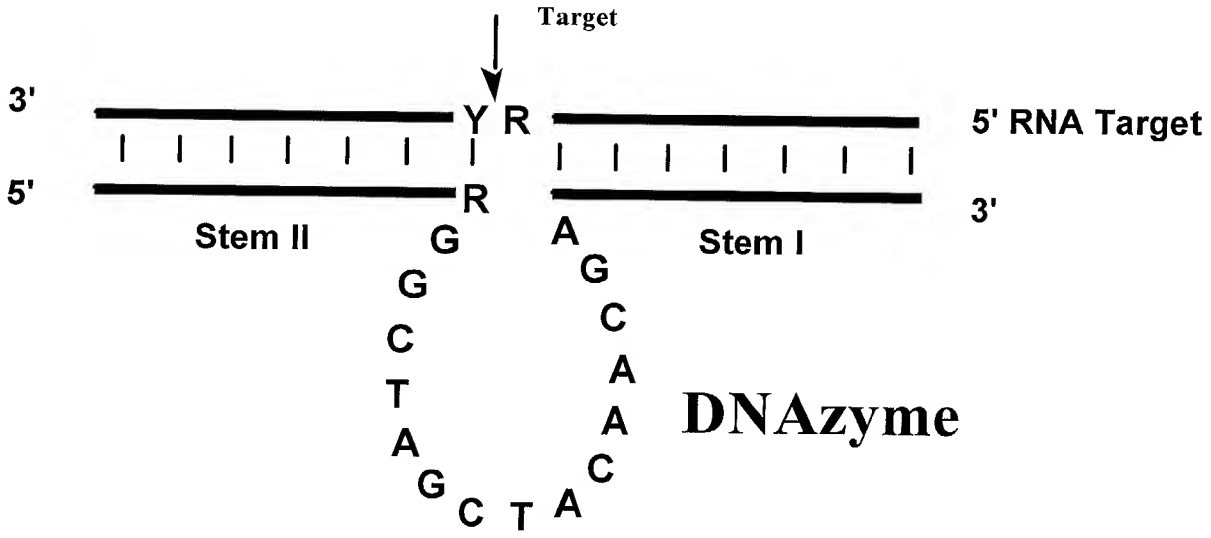
U,C = 2'-NH_2-U,C (U and C underlined)
Lower case = 2'-O-Me
Uppercase = Ribo
iB = inverted deoxy abasic



The gaa loops may be replaced with loops of differing nucleic acid compositions, or with a linker, for example an 18 atom polyethylene glycol (Spacer) or equivalent.

Phosphorothioate linkages can be introduced, for example, at the 4 terminal 5'-internucleotide linkages, to increase nuclease stability.

Figure 5: DNAzyme Motif



Legend

Y = U or C
R = A or G

FIGURE 6 Dual Reporter System for Cytoplasmic HCV Target

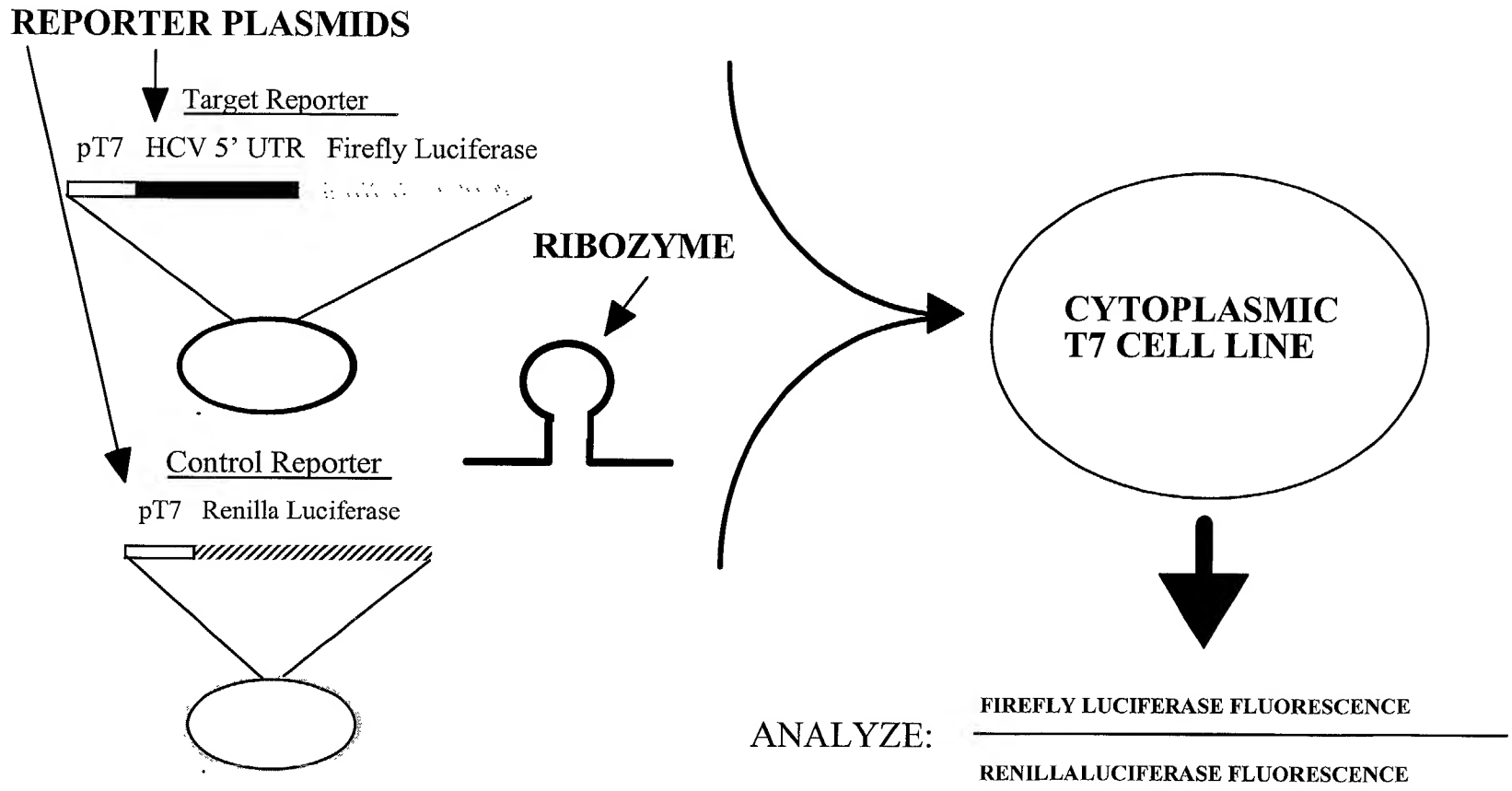


Figure 7: Secondary structure of the HCV 5'UTR

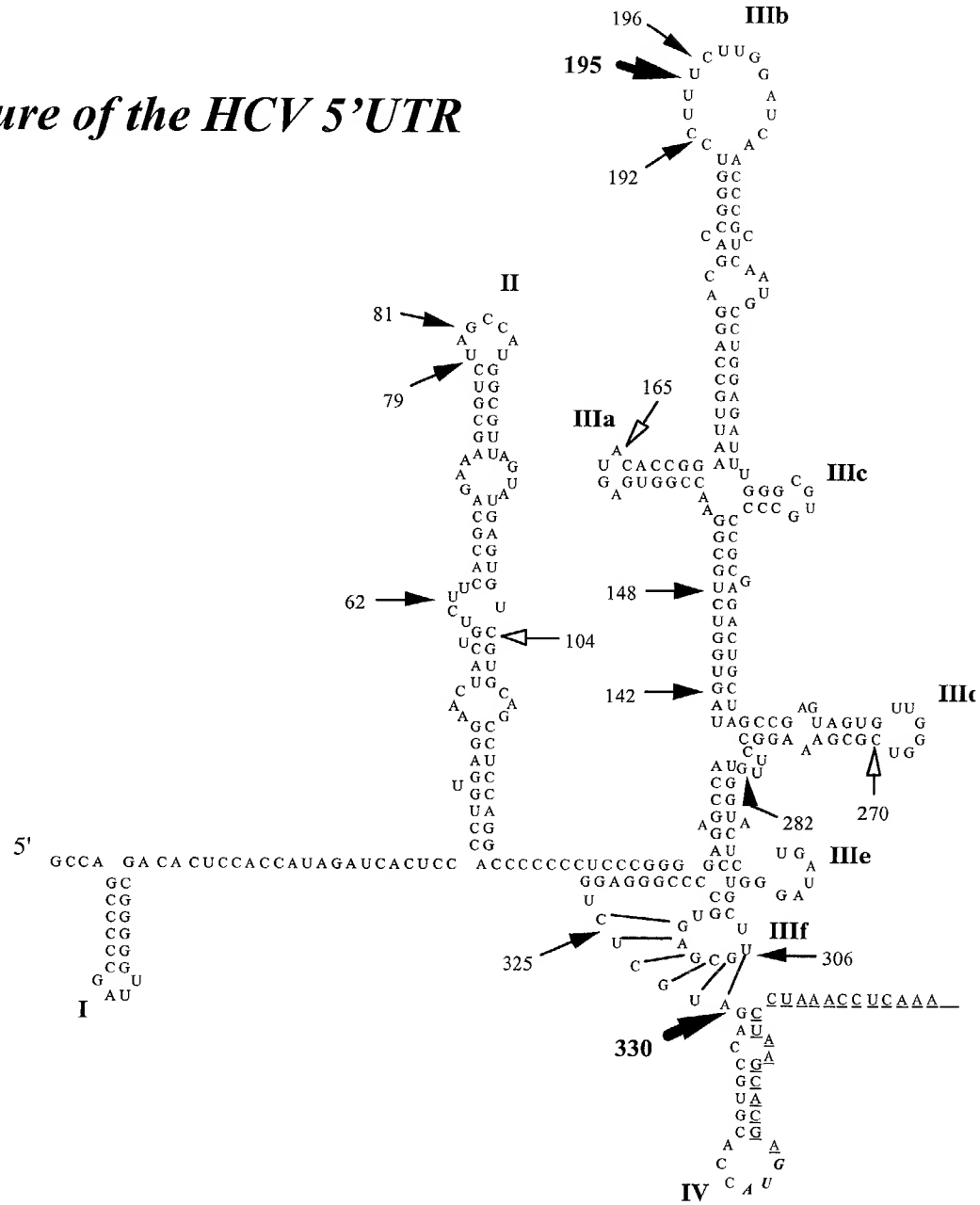
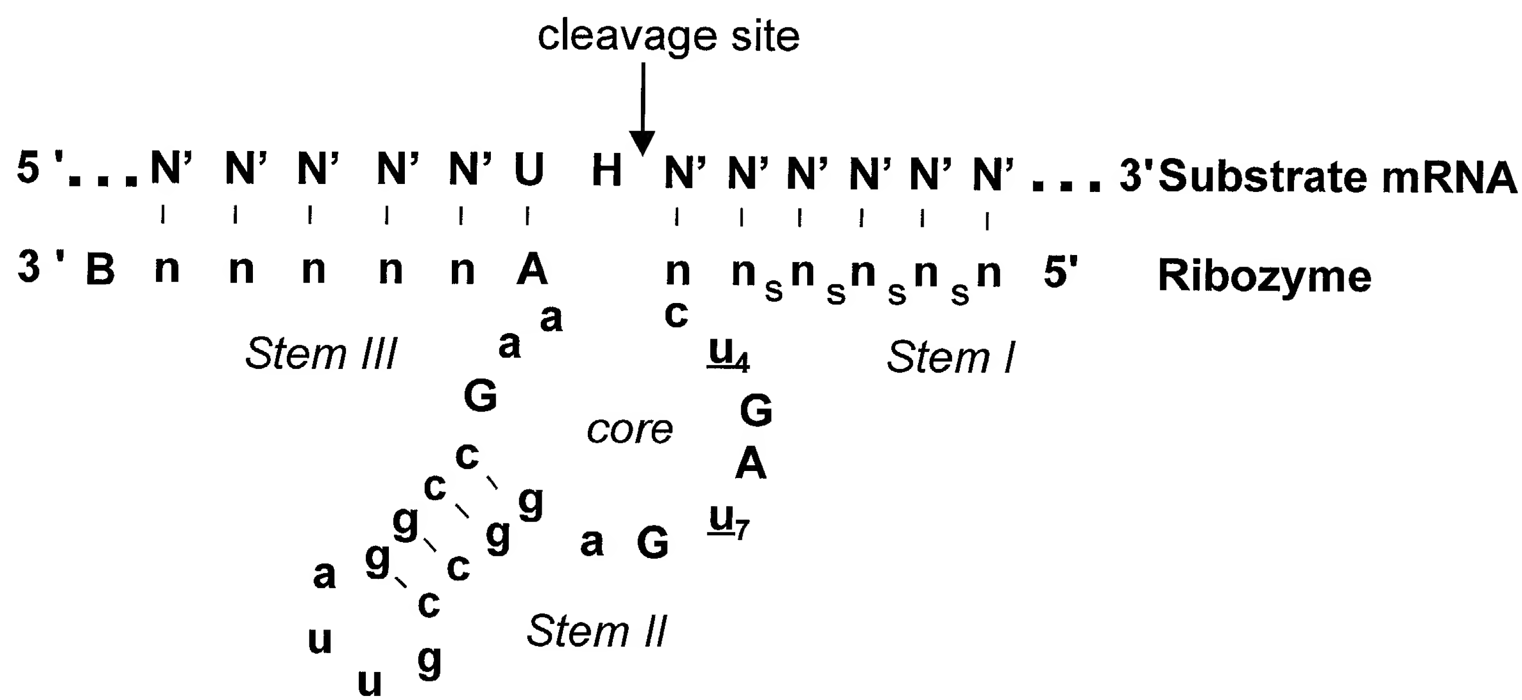


Figure 8: A Chemically Stabilized Enzymatic Nucleic Acid Molecule



UPPER CASE = RIBO nucleotide
lower case = 2'-O-methyl nucleitide
u = 2'-deoxy-2'-amino Uridine
s = phosphorothioate
B = inverted deoxyabasic moiety

Figure 9: Enzymatic nucleic acid mediated inhibition of HCV-luciferase expression

A.

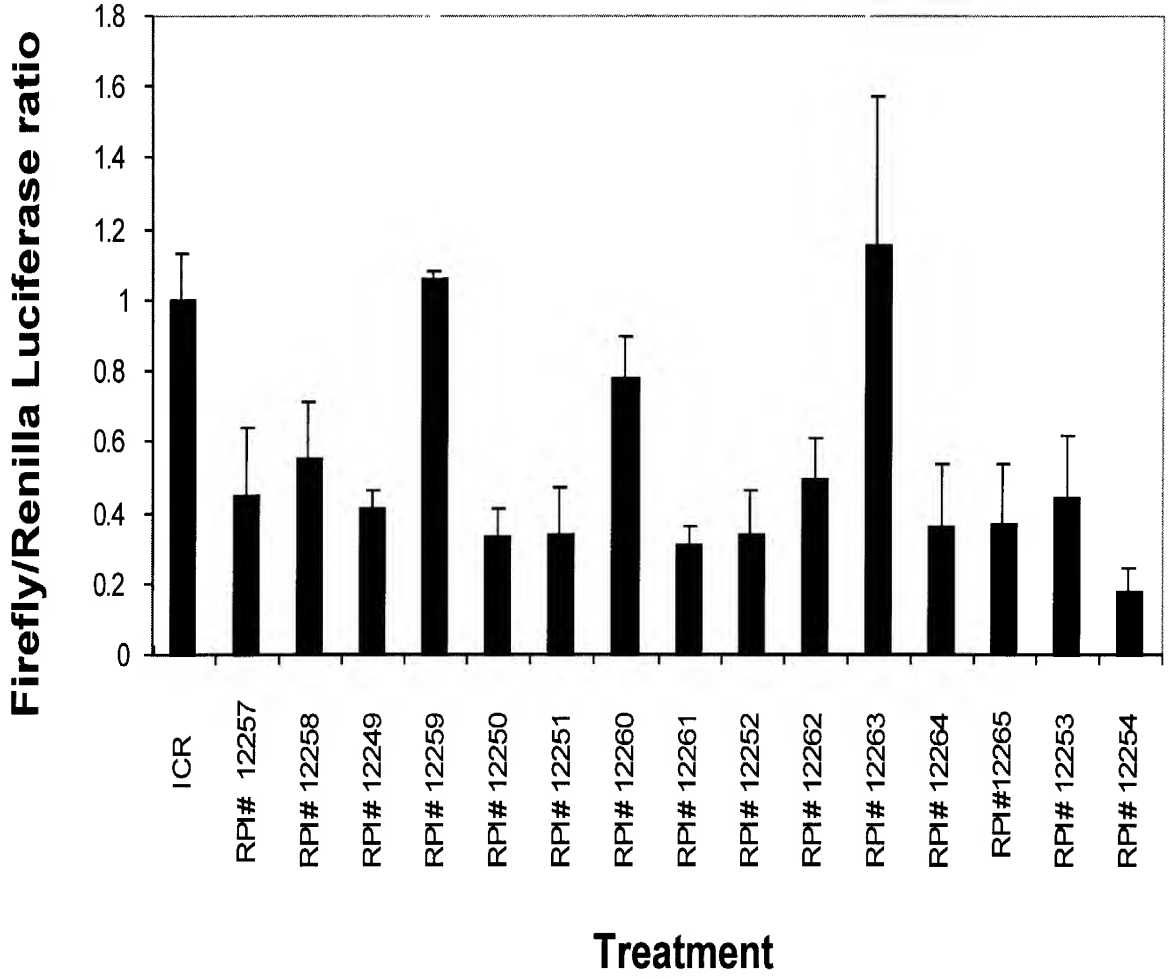


Figure 9: Enzymatic nucleic acid mediated inhibition of HCV-luciferase expression

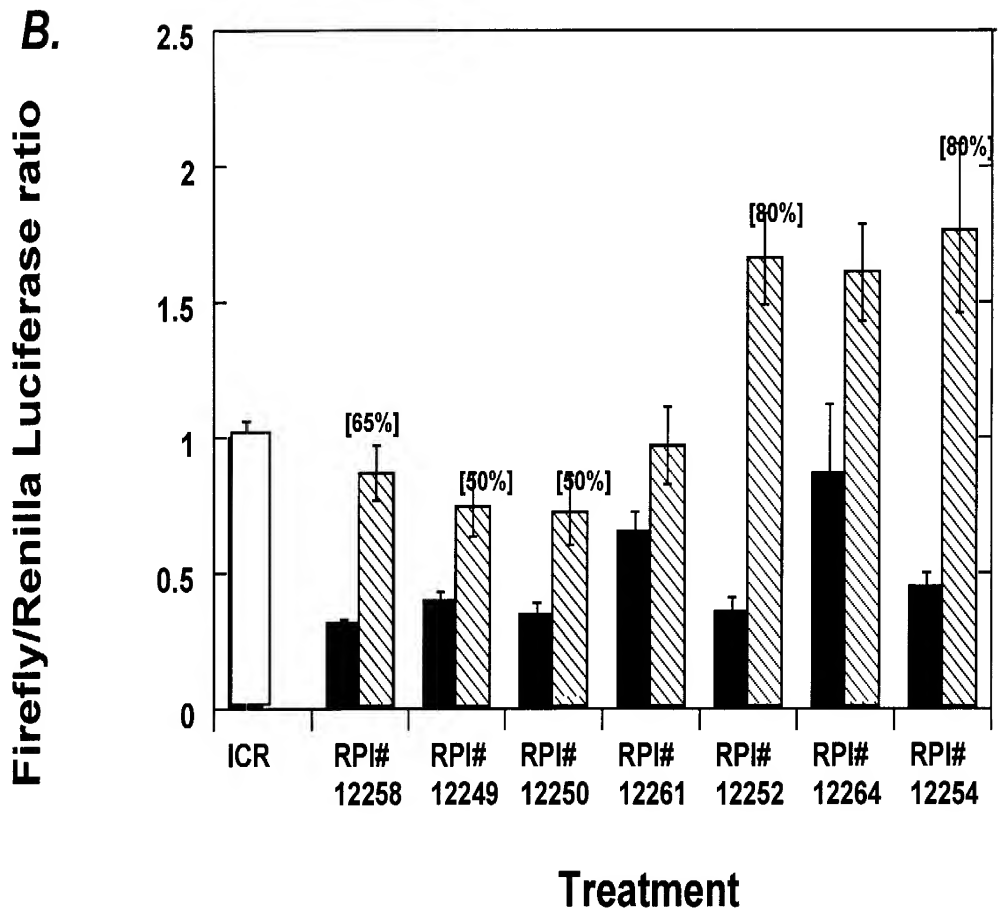


Figure 10: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

A.

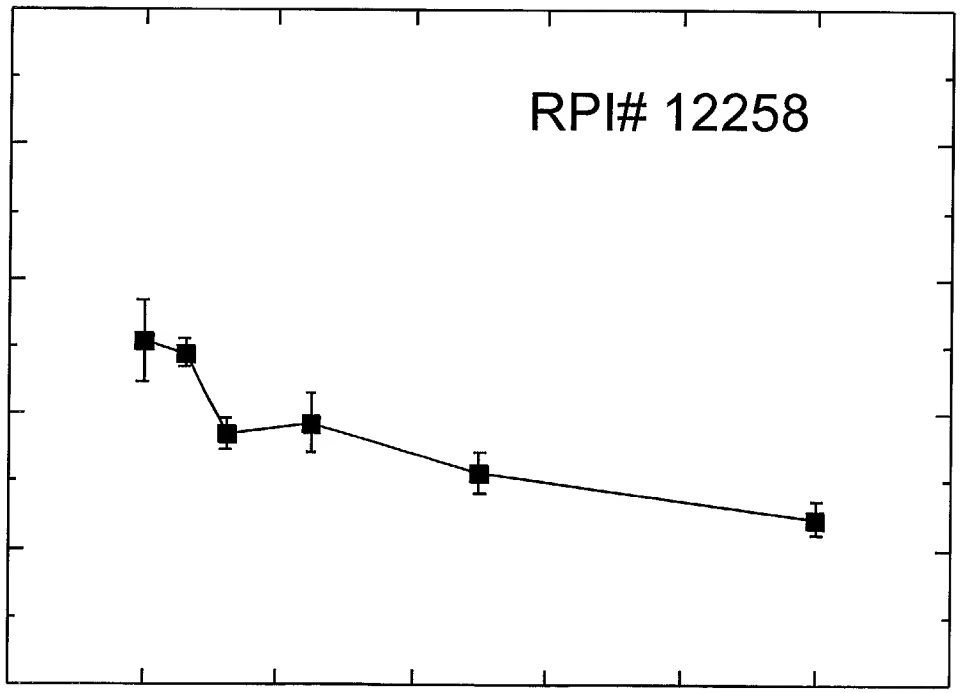


Figure 10: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

B.

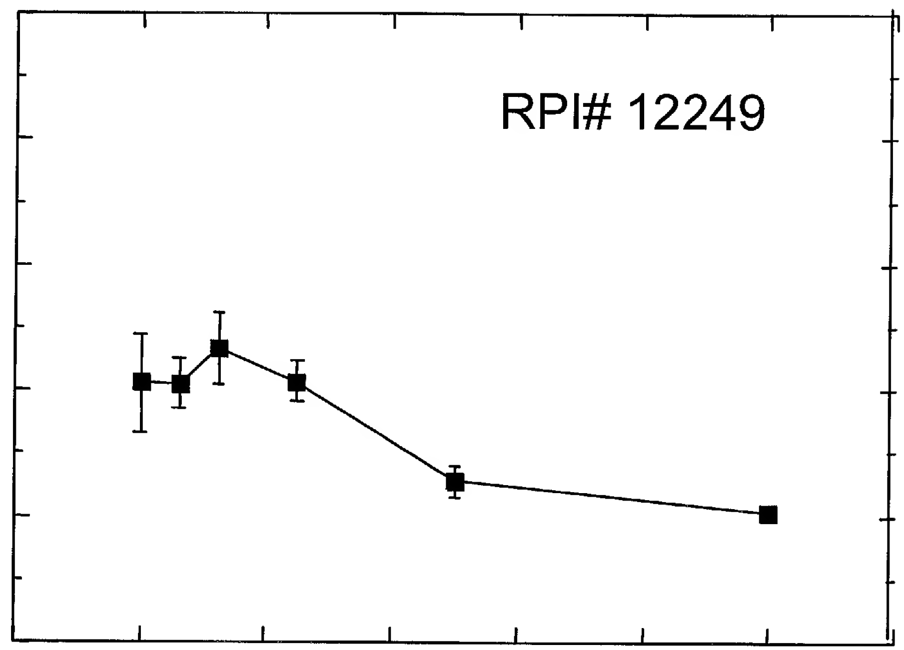


Figure 10: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

C.

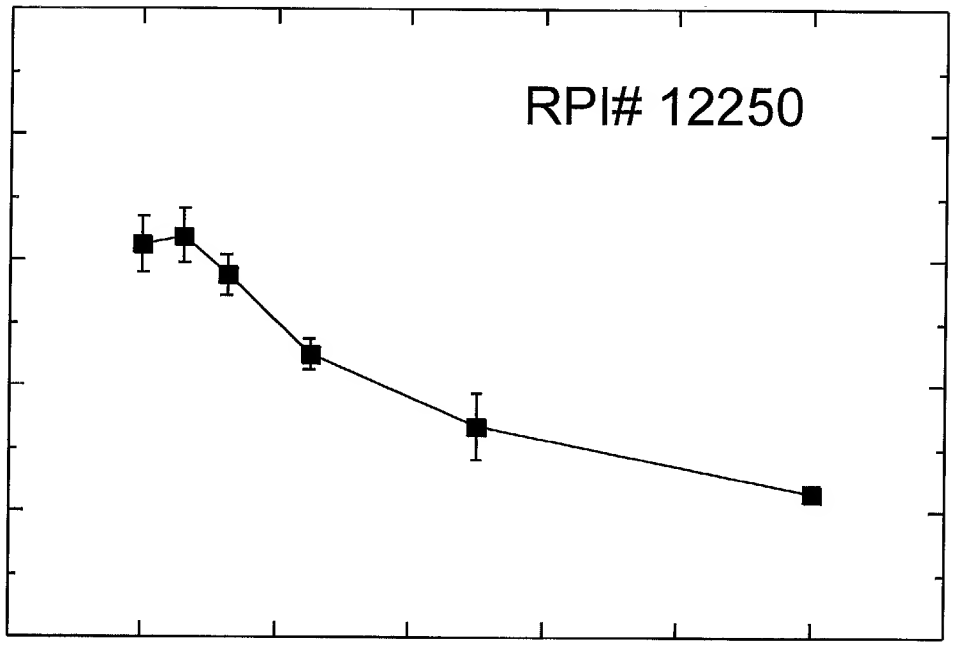


Figure 10: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

D.

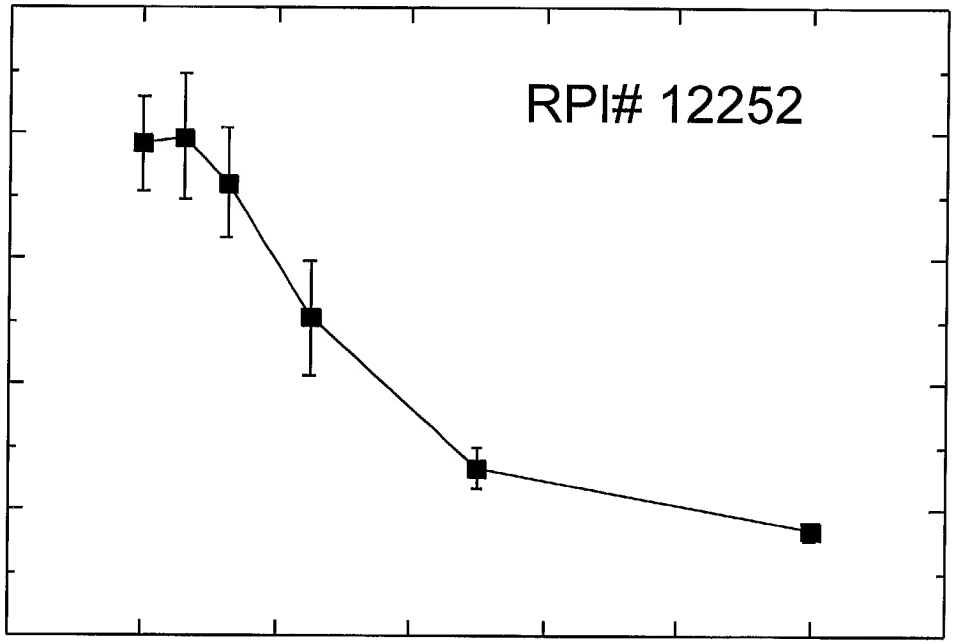


Figure 10: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

E.

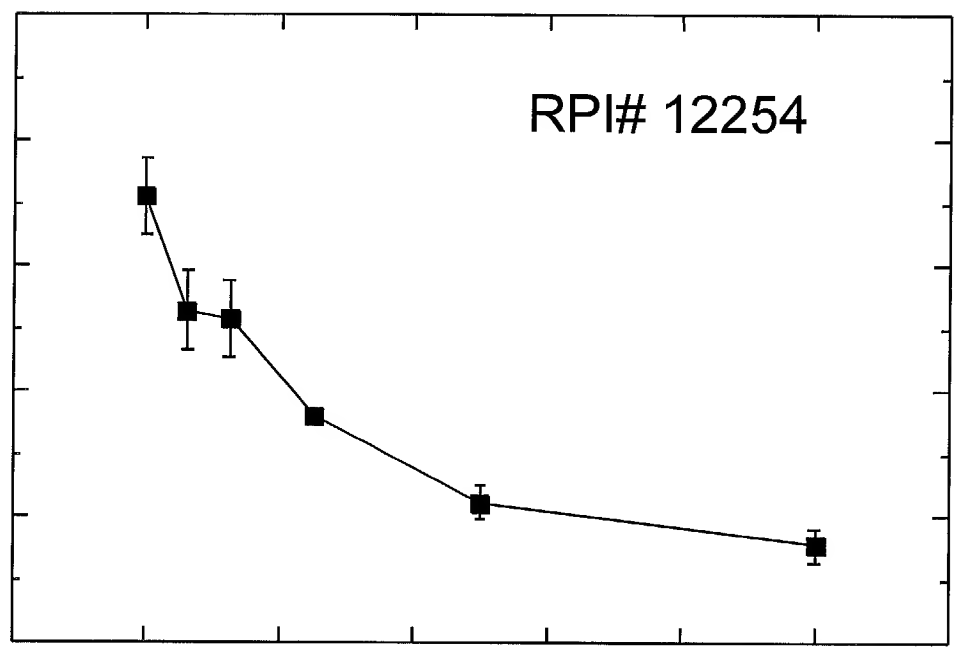


Figure 11: Enzymatic nucleic acid reduction of HCV/luciferase RNA and inhibition of HCV-luciferase expression

A.

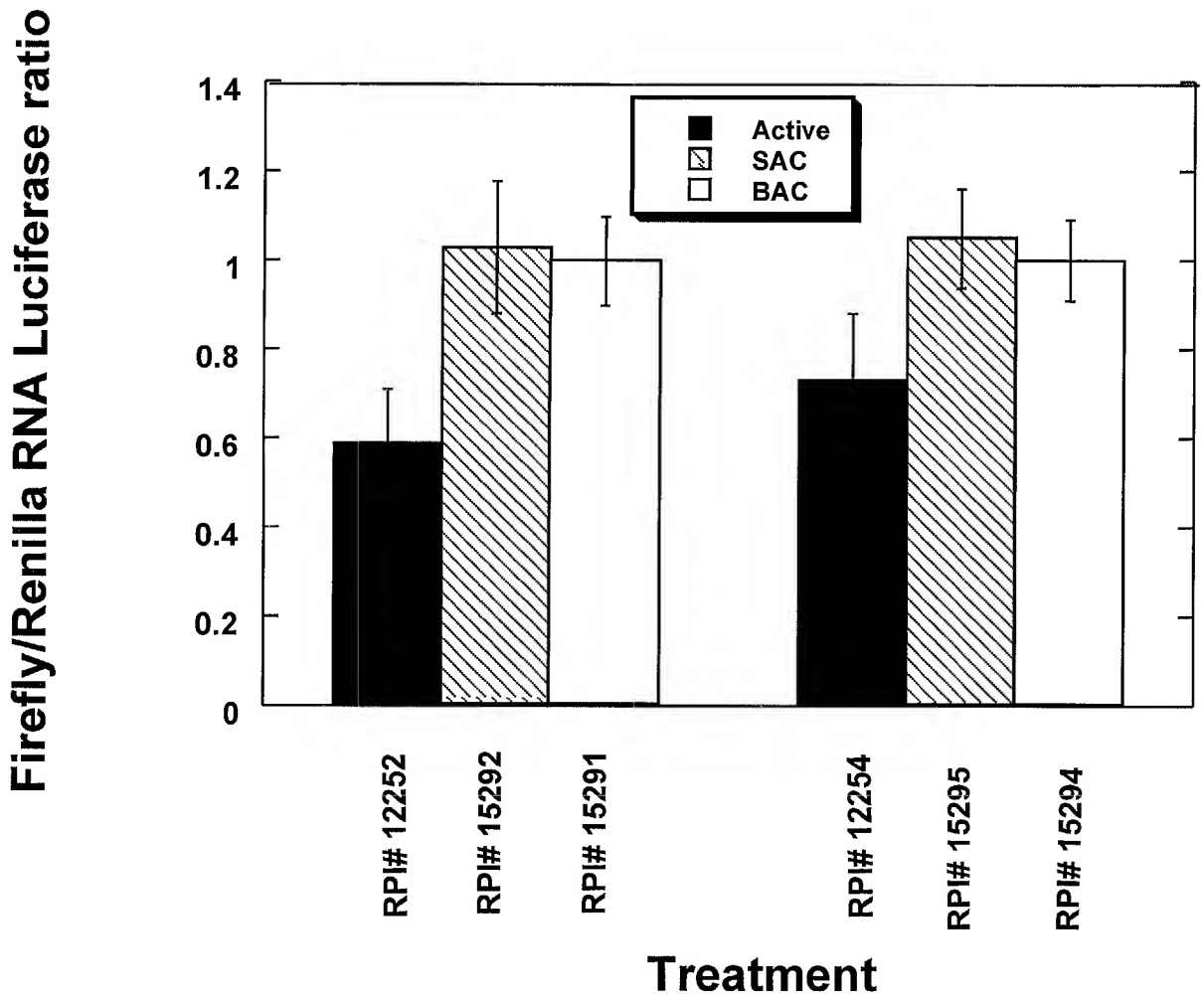


Figure 11: Enzymatic nucleic acid reduction of HCV/luciferase RNA and inhibition of HCV-luciferase expression

B.

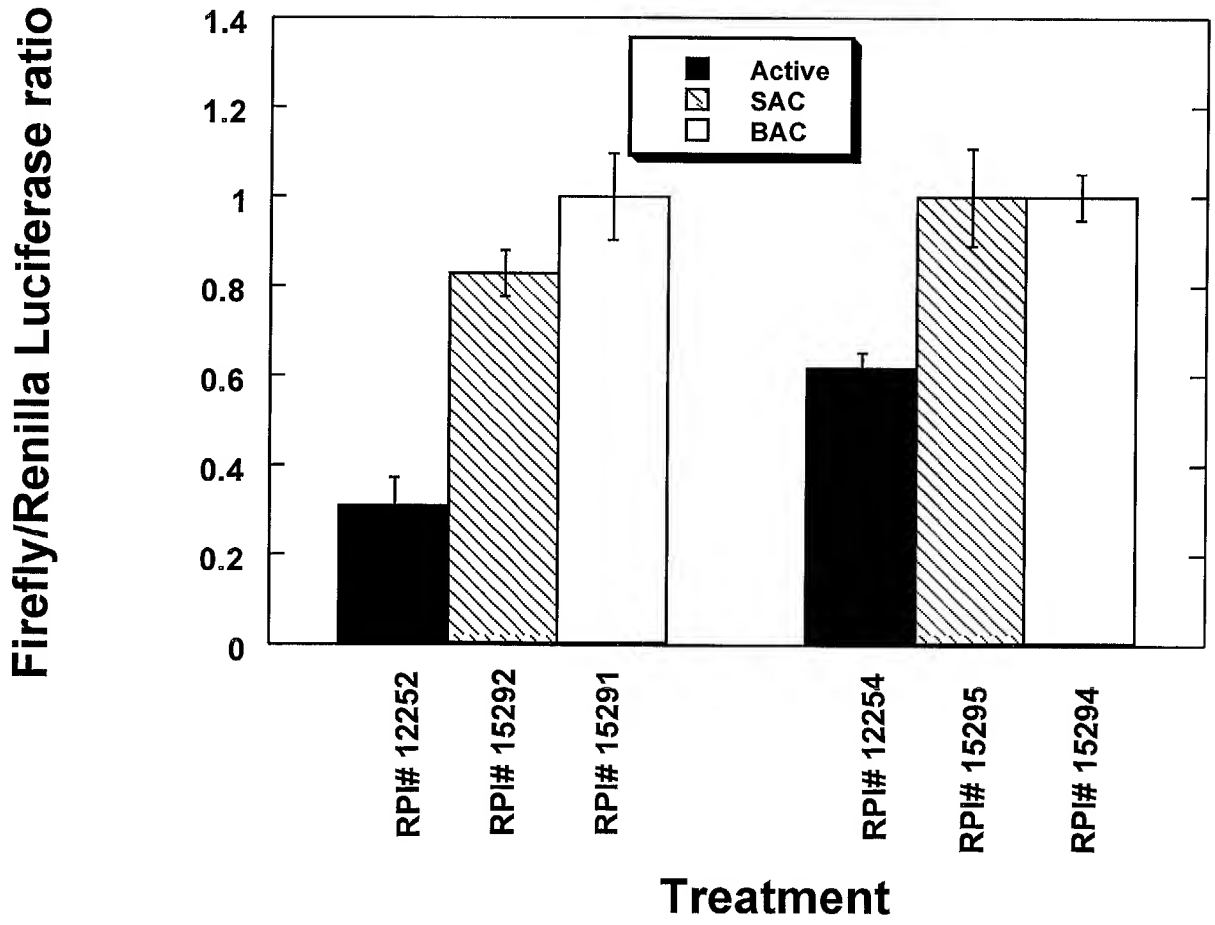
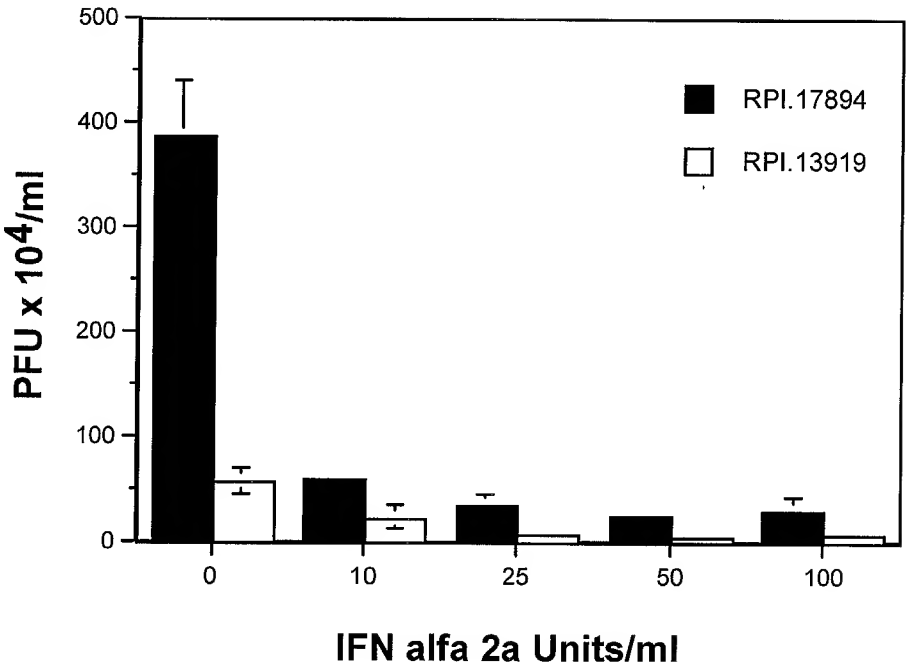
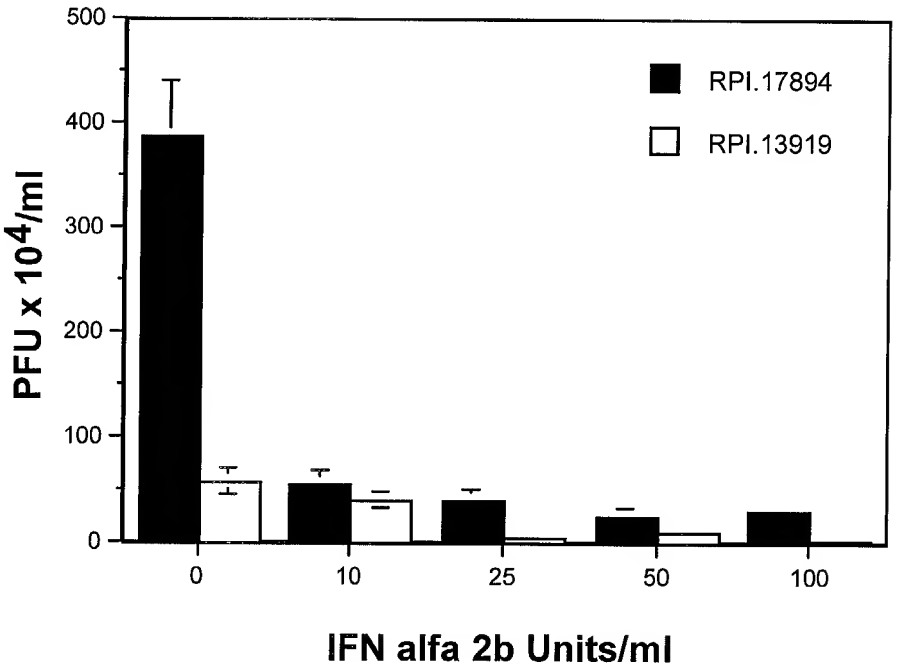


Figure 12: Interferon Dose response with Enzymatic Nucleic Acid



A.

Figure 12: Interferon Dose response with Enzymatic Nucleic Acid



B.

Figure 13: Site 195 anti-HCV enzymatic nucleic acid dose response in combination with interferon pretreatment

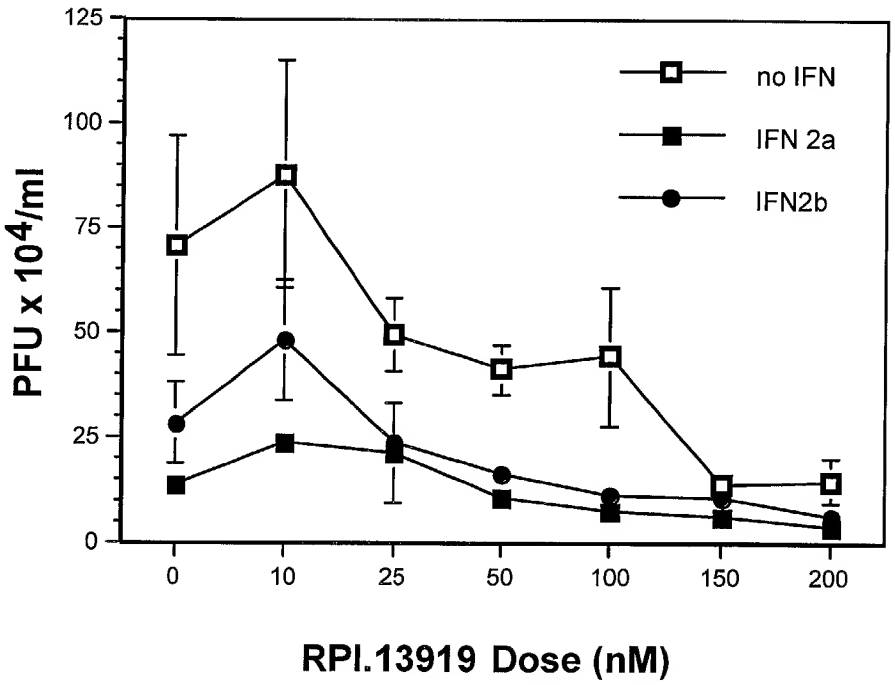


Figure 14A: CIFN dose response with site 195 anti-HCV enzymatic nucleic acid treatment

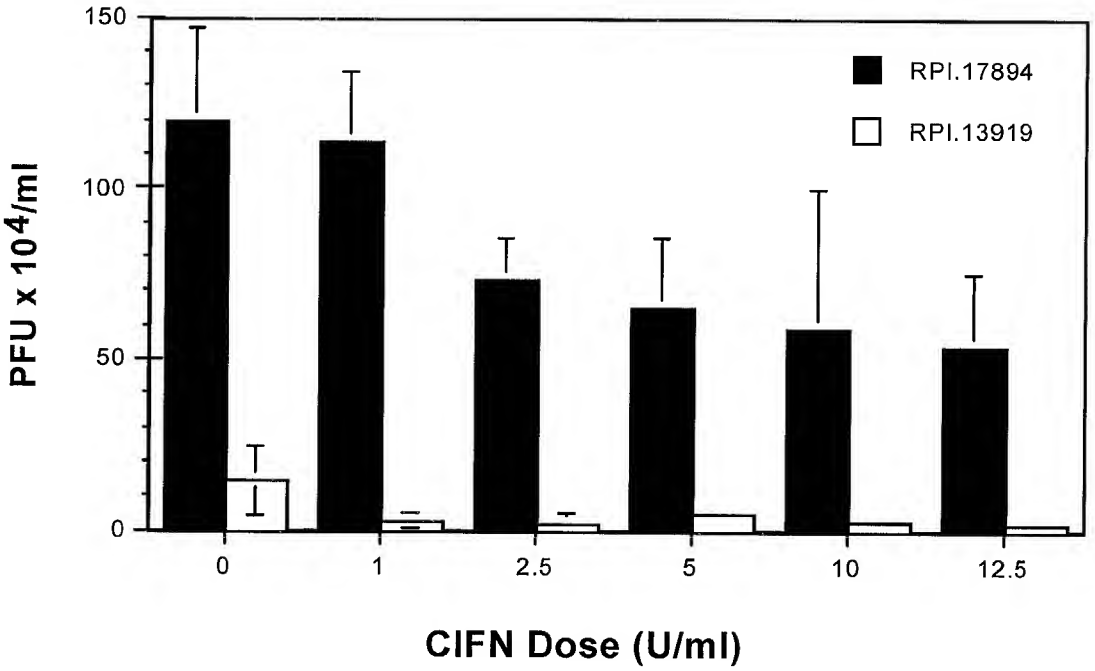


Figure 14B: Site 195 anti-HCV enzymatic nucleic acid dose response with CIFN pretreatment

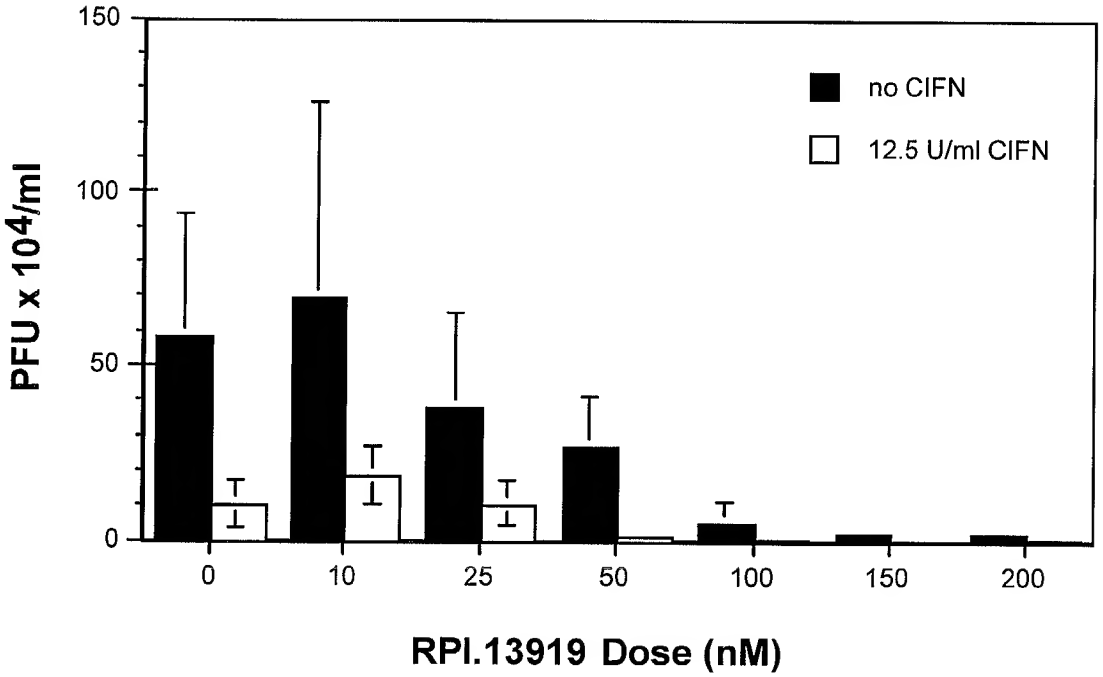


Figure 15: Enhanced antiviral effect of an anti-HCV enzymatic nucleic acid targeting site 195 used in combination with consensus interferon (CIFN)

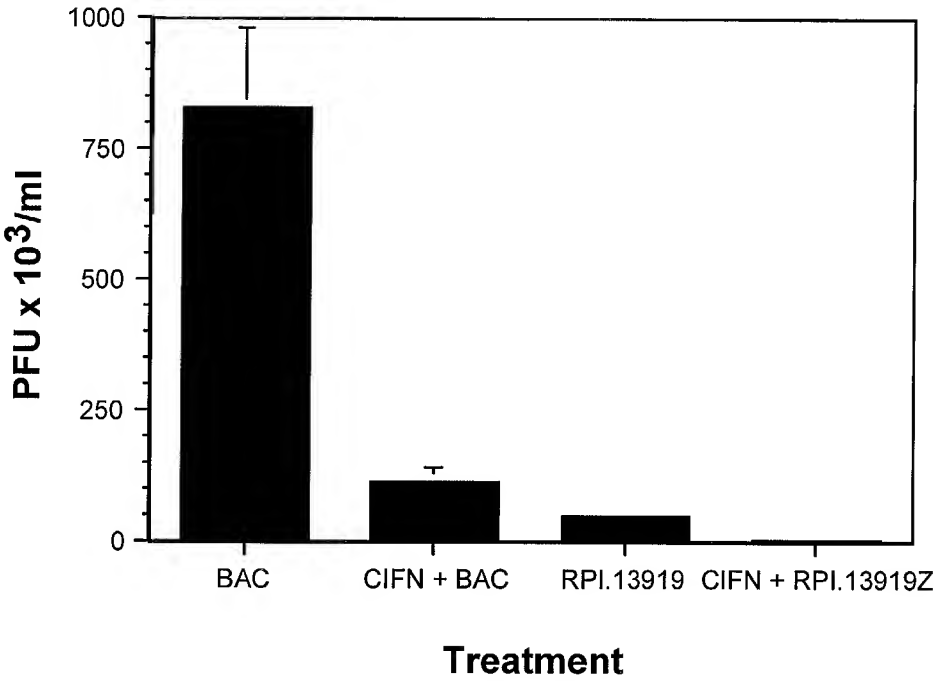


Figure 16: Inhibition of HCV-PV Replication by Zinzyme Treatment

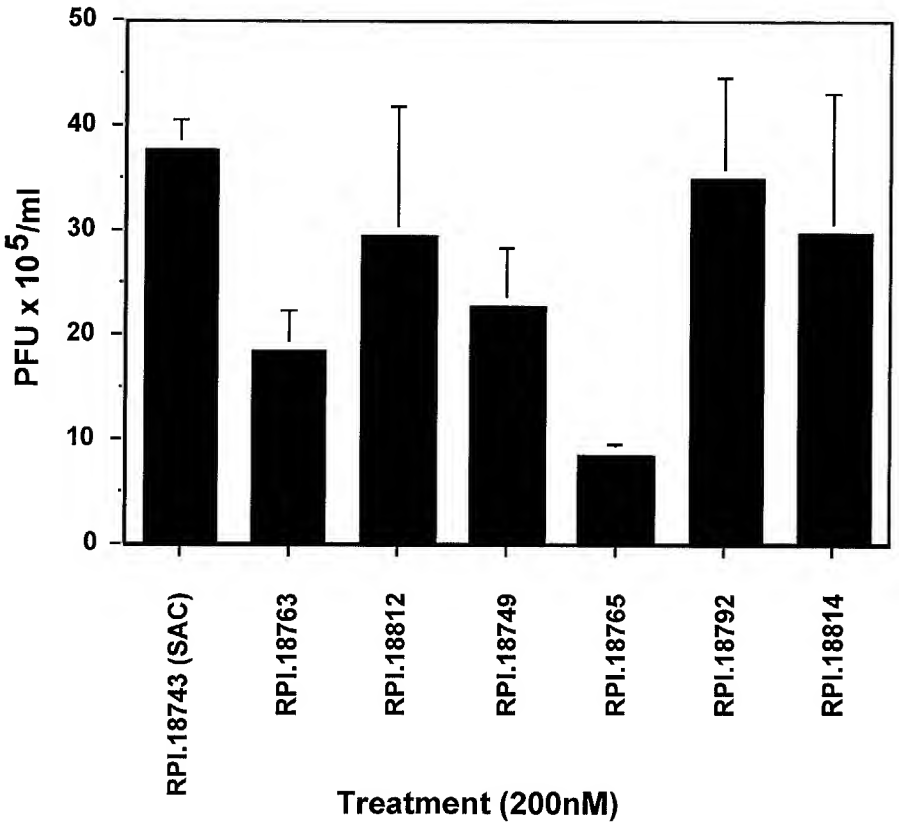


Figure 17: Inhibition of HCV-Poliovirus Replication by Antisense